

REMARKS

This Amendment and Response is submitted in response to the Office Action mailed 23 July 2003. Withdrawal of the rejection and reconsideration with an eye toward allowance is respectfully requested.

Claim Status

Claims 2, 3, 5-9, and 24-35 are pending after entry of the present amendment. Claims 2, 3, 5-9 and 24-31 stand rejected. Claims 6, 28, and 29 are amended herein, and claims 32-35 added. A complete listing of all claims that are, or were in the application, along with an appropriate status identifier, is provided above in the section entitled "Amendments to the Claims". Markings are provided on claims amended in the present amendment.

Priority

Applicant notes with appreciation the Examiner's indication that the effective filing date for the instant claims is the filing date of provisional application 60/175,539 (11 January 2000).

Applicant also notes that the Examiner indicates provisional application 60/145,840 fails to provide support for the instantly claimed biochip cartridge. Applicants do not so concede, however, for the purposes of continuing prosecution of the claims in the application, and as the filing date of the '840 application is after the filing date of the '539 application, which the Examiner concedes is a proper priority claim, Applicants will not pursue perfecting the priority claim to the '539 application at this time. Applicant reserves the right, however, to perfect this priority claim in a related application.

Claim Rejections – 35 U.S.C. §112

Claims 28 and 29 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner states that claims 28 and 29 are indefinite as they recite the trademarks Teflon™ and Gortex™, respectively. Applicant has amended claim 28 to recite the generic name "polytetrafluoroethylene" instead of "teflon". Applicant has amended claim 29 to recite the generic name "expanded-polytetrafluoroethylene" instead of "Gore-Tex™".

Claim Rejections – 35 U.S.C. §102

Claims 24, 2, 3, 5, 7, and 8 were rejected under 35 U.S.C. §102(e) as being anticipated by Burns et. al. (U.S. Patent No. 6,379,929).

Burns is directed toward microfluidic devices for performing isothermal amplification (see col. 3, lines 30-44). Preferred embodiments of microfluidic devices disclosed by Burns include a flow-directing

system employing a surface-tension-gradient mechanism. A series of heating elements are provided along a microdroplet transport channel (see col. 6, lines 46-55). Further, Burns discloses that differences in hydrophobic and hydrophilic surface structures may be employed to control the flow or transport of fluids through the device (see col. 7, lines 5-7). To this end, Burns discloses hydrophilicity-enhancing compounds and hydrophobic coatings.

In contrast, Applicant's claim 24 recites "a substrate comprising a printed circuit board comprising an array of electrodes, each electrode comprising: A) a self-assembled monolayer; and B) a capture binding ligand".

Applicant notes that, for a reference to anticipate a claim, the reference must teach every element of the claim (see M.P.E.P. §2131).

Applicant respectfully submits that Burns fails to disclose an array of electrodes, each electrode comprising a self-assembled monolayer and a capture binding ligand. Burns discloses a self-assembled monolayer coating (col. 26, lines 59-61) for treating the surface of channels. Applicant submits that this is not disclosure of an array of electrodes comprising a self-assembled monolayer. Burns discloses that the channels are made of diffused silicon on the bottom and a thin film cap on the top (see col. 26, lines 51-52). On the top layer, a set of thin film electrodes and heaters is constructed (see col. 26, lines 54-55). The surface treatment of the channels may be done by immersing the open channel in organosilane or a self-assembled monolayer coating, with oxygen reactive ion etching removing the surface from unwanted areas (see col. 26, lines 59-62). Applicant submits that Burns therefore discloses a channel, portions of which may be treated with a self-assembled monolayer coating. Burns does not disclose or suggest an electrode comprising a self-assembled monolayer.

Further, Burns does not disclose or suggest an electrode comprising a capture binding ligand. Burns discloses reagents for an isothermal nucleic acid amplification reaction (see col. 47, lines 1-34). One or more of the reagents may be operably or functionally connected to the microfabricated substrate (see col. 47, lines 12-26). Burns does not disclose an electrode comprising a capture binding ligand.

Claims 2, 3, 5, 7, and 8 depend from and include all limitations of Applicant's claim 24. Accordingly, Applicant submits that the 35 U.S.C. §102(e) rejection of claims 24, 2, 3, 5, 7, and 8 over Burns is improper and should be withdrawn.

Claim Rejections – 35 U.S.C. §103

Claims 2-3 and 5-8 were rejected under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter et. al. (WO 98/12539) in view of Schembri et. al. (U.S. Patent Number 6,258,593).

Wohlstadter discloses supports having a plurality of binding domains (see, for example, Wohlstadter, page 17, lines 32-33). A plurality of electrodes are disclosed which are able to trigger electrochemiluminescent emission from a binding domain (see, for example, Wohlstadter, page 18, lines 4-7).

Schembri et. al. disclose an apparatus for conducting chemical or biochemical reactions on a solid surface within an enclosed chamber (see Schembri, abstract). After a reaction is performed, an array may be read with a confocal scanner (see Schembri, col. 18, lines 28-31. Schembri does not disclose self-assembled monolayers. Further, Schembri discloses a method for mixing with a bubble in a chamber and methods to ensure a bubble is contained within a chamber.

In contrast, Applicant's amended claim 6 recites an inlet port positioned at the bottom of the reaction chamber for the introduction of reagents, and an outlet port positioned at the top of the reaction chamber to minimize the introduction or retention of air bubbles upon introduction of reagents.

Applicants note that, to establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference teachings. Further, the cited art reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §2142).

Applicants respectfully submit that Wohlstadter and Schembri fail to provide the required motivation to combine the references. The Examiner states that it would have been obvious to combine the teachings for the expected benefit of improving and facilitating reagent mixing. The Examiner points to Schembri et. al. (col. 12, lines 25-42), where Schembri discloses that, if the surfaces of the chamber are rendered wettable by the inclusion of a surfactant, it is possible to leave a bubble inside the chamber. Inclusion of surfactant sufficient to allow movement of a bubble in the reaction chamber significantly improves mixing in the reaction chamber when a bubble is present and the chamber is moved or rotated so as to move the bubble (see col. 12, lines 25-26 and 30-34). Accordingly, Schembri apparently motivates the addition of surfactant to enhance mixing in a reaction chamber. Applicant can respectfully find no specific motivation in the cited references to combine this technique with the cassettes of Wohlstadter having plurality of electrodes which are able to trigger electrochemiluminescent emission from a binding domain (see, for example, Wohlstadter, page 18, lines 4-7). The advantages Schembri discloses regarding improvement of mixing occur when the chamber is moved or rotated so as to move the bubble. The cassettes of Schembri are inserted into a housing (see FIG. 47). It is unclear as to how one would move or rotate the chamber during its apparently fixed insertion into this housing to achieve the results disclosed by Schembri. Accordingly, Applicants submit that the 35 U.S.C. §103(a) rejection of claim 6 is improper.

Moreover, Applicants submit that Wohlstadter and Schembri, alone or in combination, fail to disclose all limitations of Applicants' amended claim 6.

As per claim 6, Applicants respectfully submit that Schembri does not disclose a chamber designed to minimize the introduction or retention of air bubbles, but rather a chamber designed to retain an air bubble and conduct mixing with the bubble (see Schembri, col. 25, lines 25-42). Accordingly, Applicants respectfully submit that Schembri teaches away from Applicants' claim 6 by disclosing the advantageous use of a bubble. A reference which leads one away from the claimed invention cannot render the invention obvious. See *Dow Chemical v. American Cyanamid*, 2 USPQ 2d 1350 (Fed. Cir.

1987). In particular, Applicant's claim 6 recites an inlet port positioned at the bottom of the reaction chamber for the introduction of reagents and an outlet port positioned at the top of the reaction chamber to minimize the introduction or retention of air bubbles upon introduction of reagents. Schembri and Wohlstadter do not disclose this structure (see, for example, Schembri FIG. 1 and Wohlstadter FIG. 1). Accordingly, the combination of references do not teach or suggest all limitations of Applicant's claim 6, and the 35 U.S.C. §103(a) rejection should be withdrawn.

Claims 2, 3, 5, 7, and 8 depend from and include all limitations of Applicant's claim 6. Accordingly, for at least the reasons described above, the 35 U.S.C. §103(a) rejection of claims 2-3 and 5-8 over Wohlstadter in view of Schembri is improper and should be withdrawn.

Claims 9 and 25-31 were rejected under 35 U.S.C. §103(a) as being unpatentable over Burns et al in view of Anderson et al (U.S. Patent Number 6,326,211).

Burns is discussed above.

Anderson discloses a device for performing sample acquisition and preparation operations (see Anderson, col.5, lines 12-14). Data is gathered from the array by exciting fluorescently labeled targets (see Anderson, col. 16, lines 62-65).

In contrast, Applicants' independent claim 26 recites an array of electrodes, each electrode comprising a self-assembled monolayer and a capture binding ligand. Claim 26 further recites an inlet port for the introduction of reagents, said inlet port comprising a valve including a semipermeable membrane.

As stated above, to establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference teachings. Further, the cited art reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §2142).

Applicants respectfully submit that Burns and Anderson fail to provide the required motivation to combine the references. The Examiner suggests that the motivation would be for the expected benefit of controlling fluid flow (see office action, page 12). Applicants respectfully submit that an advantageous result of the use of a valve, as disclosed by Burns, is not necessarily a motivation to combine that valve with the disclosure of Anderson. "The mere fact that it is possible to find two isolated disclosures which might be combined in such a way to produce a new compound does not necessarily render such production obvious unless the art also contains something to suggest the desirability of the proposed combination." *In re Bergel*, 130 USPQ 206, 208 (CCPA 1961). Applicants submit that no specific motivation has been provided to combine a vent, as disclosed by Anderson, with the fluid manipulation system of Burns. Accordingly, Applicants submit that the 35 U.S.C. §103(a) rejection of claim 26 is improper and should be withdrawn.

Further, Applicants submit that neither Burns nor Anderson, nor the references in combination, disclose or suggest all limitations of Applicant's claim 26. As described above, Applicant submits that

Burns fails to disclose or suggest an array of electrodes, each electrode comprising a self-assembled monolayer and a capture binding ligand. Anderson similarly fails to disclose these features. Further, while Anderson discloses a vent, Anderson fails to disclose or suggest an "inlet port comprising a valve including a semipermeable membrane", as recited in Applicant's claim 26. The vent of Anderson is positioned in an area away from the inlet port (see, for example, FIG. 2B). Accordingly, Applicant's submit that the cited references fail to disclose or suggest all limitations of Applicant's claim 26, and therefore the 35 U.S.C. §103(a) rejection of claim 36 over Burns in view of Anderson should be withdrawn.

Claims 9, 25, and 27-31 depend from and include all limitations of Applicant's claim 26. Therefore, at least for the reasons described above, the 35 U.S.C. §103(a) rejection of claims 9 and 25-31 should be withdrawn.

Claim 9 was further rejected under 35 U.S.C. §103(a) as being unpatentable over Wohlstadter in view of Schembri as applied to claim 6 and further in view of Anderson.

Wohlstadter, Schembri, and Anderson have been described above.

As stated above, to establish a prima facie case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference teachings. Further, the cited art reference (or references when combined) must teach or suggest all the claim limitations. (See M.P.E.P. §2142).

Applicants submit that the required motivation to combine the references has not been provided. Applicant's argument with respect to the combination of Wohlstadter and Schembri as applied to claim 6 are discussed above with reference to claim 6. The Examiner suggests that the further motivation to combine the teachings of Anderson would be for the expected benefits of easy access to reagents and convenient storage of reagents as taught by Anderson. The Examiner cites a section of Anderson (col. 25, lines 42-52) that discusses storing reagents in solid or liquid form in a chamber adjacent to a sample collection chamber, as a particular pump has been provided to move these reagents from the adjacent chamber into the collection chamber. Applicants respectfully submit that disclosure of an adjacent storage chamber for reagents does not itself provide motivation to combine that adjacent storage chamber with the cassette of Wohlstadter. Accordingly, Applicant submits that a proper motivation to combine has not been provided and the 35 U.S.C. §103(a) rejection is improper.

Further, Applicants submit that the combination of references fail to disclose all limitations of Applicant's claim 9, which recites "a cap comprising at least one storage well comprising assay reagents". The Examiner concedes that Wohlstadter does not teach such a cap (see office action, page 8). Applicant submits that Schembri also fails to disclose such a cap. The Examiner suggests that Anderson teaches a cap, referring to well #510 in Anderson's Fig. 5B. Applicants respectfully submit that Anderson merely discloses a well for holding reagent, and not a cap, as recited by Applicant's claim 9. Accordingly,

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Applicant submits that the 35 U.S.C. §103(a) rejection of claim 9 over Wohlstadter in view of Schembri in further view of Anderson is improper and should be withdrawn.

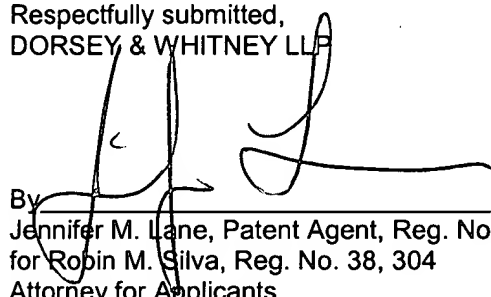
New Claims

Applicant has added new claims 32-35 which further distinguish over the cited art. For example, claims 32 and 33 recite further limitations regarding the inlet and outlet ports. Claim 34 recites a removable cap and claim 35 is directed toward a method of filling a reaction chamber.

CONCLUSION

Applicants submit the claims are in condition for allowance, and notification of such is respectfully requested. If after review, the Examiner feels there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,
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